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Penile granulomatosis presenting as pseudoangioedema

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Summary
Many conditions may present as angioedema. We report a case of a 46 year-old man presenting with intermittent episodes of penile swelling. Following a series of investigations, he was diagnosed with genital granulomatosis. Ano-genital granulomatosis is a rare chronic inflammatory condition and that can present as diffuse penile, scrotal, vulvar or ano-perineal swelling with non-caseating non-necrotising granulomas on histology.

Introduction

A variety of conditions may present with swelling mimicking angioedema. Determining the cause of the swelling can be challenging and requires a thorough history together with appropriate investigations. Correct identification of the possible cause can help to target treatment appropriately.

Case Report

A 46 year-old man was referred to the Clinical Immunology clinic with a six-year history of intermittent penile swelling. These episodes occurred on average five times a year. Initially he would feel extremely unwell, cold, experience rigors and a headache. Subsequently, penile swelling would appear associated with difficulty in passing urine. The swelling would then persist for several weeks. Progressively it would remain for longer periods of time.
He had a past medical history of Type I diabetes mellitus. He had an episode of lip swelling 11 years prior that was attributed to lubricating wax in vitamin tablets. No further investigations were carried out at the time and it did not recur. He was on insulin, simvastatin and ramipril. Ramipril was stopped but the episodes of swelling continued.
Physical examination revealed significant penile oedema with a thickened indurated area on the dorsal penis. There was no lymphadenopathy, mouth or genital ulcers. Respiratory and abdominal examinations did not reveal any abnormalities.
Initial laboratory investigations revealed normal full blood count, erythrocyte sedimentation rate, C-reactive protein, albumin, total protein, immunoglobulins, lactate dehydrogenase, C3 and C4 complement levels. Anti-neutrophil cytoplasmic antibodies (ANCA) were negative. A screen for sexually transmitted infections including syphilis was negative. Genetic testing for periodic fever syndromes did not reveal any abnormalities.
Following dermatological review, he was started on penicillin V 500mg twice daily for possible lymphoedema associated cellulitis. Furthermore, patch testing in order to assess possible contact allergens revealed an isolated positive response to econazole which was not of current relevance.

Ultrasound scan of the abdomen/pelvis and cystoscopy did not reveal any abnormality. A deep skin biopsy of the penile shaft showed a perivascular infiltrate of lymphocytes and plasma cells adjacent numerous well-formed non-caseating non-necrobiotic granulomas and macrophage giant cells. There was no vasculitis. Stains for acid and alcohol-fast bacilli and fungal organisms were negative. There was no evidence of polarizing foreign material or ruptured cysts/follicles.

The differential diagnosis of non-caseating non-necrobiotic granulomas includes conditions such as sarcoidosis and Crohn's disease. Chest X-ray, angiotensin converting enzyme and calcium levels were within the normal range. Crohn's disease was excluded following a colonoscopy with normal colonic and terminal ileum biopsies and normal small bowel MRI scan.

He responded well to treatment with prophylactic penicillin for six months with the swelling significantly subsiding and no further episodes occurring.

Discussion

Ano-genital granulomatosis is a rare chronic inflammatory condition that can present as diffuse penile, scrotal, vulvar or ano-perineal swelling. Histological appearances consist of non-caseating non-necrotising granulomas and lymphoedema. Other microscopic findings include hyperplasia and oedema of the epidermis and dermis, and irregular fibrosis in long-standing lesions.

Ano-genital granulomatosis may be regarded as the counterpart of orofacial granulomatosis (1, 2). This is thought to represent a spectrum of disease varying from localised granulomatous inflammation of the lips presenting as non-tender recurrent labial swelling that may eventually become persistent (granulomatous cheilitis, Miescher cheilitis), through orofacial swelling with mucosal ulceration to disease with neurologic deficit and lingual fissuring known as Melkersson-Rosenthal syndrome (3).

It is important that patients with suspected ano-genital granulomatosis undergo a careful diagnostic assessment. Particularly in children and young adults, this finding should alert clinicians to the possibility of Crohn's disease. Long-term follow-up for possible development of Crohn's disease should ensue (4, 5). Isolated cases of sarcoidosis, Hodgkin's lymphoma and Behçet's disease have also been reported to cause this (6).

The aetiology remains unknown, making treatment difficult. The clinical outcome can be unpredictable. Topical, intra-lesional and systemic steroids have been used. Clofazamine, azathioprine, low dose thalidomide and tacrolimus have been reported to help in small numbers of patients with orofacial granulomatosis (3). It has been suggested that chronic infection of the skin and genitalia may play a role in the appearance of lymphoedema and antibiotic treatments have been used effectively as was also the case in our patient (6).

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